

**TRANSVAGINAL ULTRASOUND AND DIGITAL  
EXAMINATION FOR PREDICTING SUCCESSFUL  
LABOUR INDUCTION IN POSTTERM PREGNANCY**

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Induction in Postterm Pregnancy**

By

Sujata Chandra

A thesis submitted in partial fulfillment of the requirements for the degree of

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Date \_\_\_\_\_



## **ABSTRACT**

**Objective:** To compare transvaginal ultrasound and digital cervical examination in predicting successful induction in post-term pregnancy.

**Methods:** Transvaginal ultrasound and digital examinations were performed on 122 women at 41 or more weeks' gestation, immediately before labor induction. Ultrasound assessments of cervical length, dilatation, and presence of funneling were compared with the components of the Bishop score. The primary outcome was the rate of vaginal delivery. Secondary outcomes included the rates of active labor in 12 hours, vaginal delivery in 12 and 24 hours, mean duration of latent phase labour, and induction to vaginal delivery interval. Linear and logistic regression models were generated to identify factors independently associated with successful induction.

**Results:** No ultrasound characteristic predicted primary or secondary outcomes. Bishop score, cervical position, and maternal age independently predicted vaginal delivery. Maternal weight, cervical dilatation, and effacement independently predicted active labor in 12 hours. Independent predictors of vaginal delivery in 12 hours were induction method, dilatation, gravidity, and maternal weight. Cervical effacement and parity independently predicted vaginal delivery in 24 hours. Maternal weight, cervical position, dilatation were independently associated with latent phase duration. Factors associated with induction to delivery interval were parity, effacement, and maternal weight.

**Conclusion:** Transvaginal ultrasound does not predict successful labor induction in post term pregnancy as well as digital cervical examination.



## **Dedication**

For my family.



## ACKNOWLEDGEMENTS

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## CHAPTER 1: Introduction

### Introduction

Labour induction is a common obstetrical intervention, and refers to the artificial initiation of uterine contractions prior to the onset of spontaneous labour. Approximately twenty percent of Canadian women have labour induced, for maternal or fetal indications.<sup>1</sup> Maternal indications for labour induction largely centre around maternal complications of pregnancy, the most common being hypertension, diabetes and collagen vascular diseases such as lupus and antiphospholipid syndrome. Common fetal indications include non-reassuring fetal status, growth restriction, oligohydramnios, premature rupture of membranes at term and clinical chorioamnionitis. Labour induction is also offered to facilitate delivery in situations of fetal demise. Less frequently, induction may be offered in circumstances where there is no maternal or fetal indication, but rather for social reasons such as geographic distance from maternity services, or risk of precipitous delivery.

Induction of labour is considered in circumstances where the risk of pregnancy prolongation is greater than the risks of induction. Risks of labour induction include risks of generating excessive uterine activity, operative delivery, and failed induction.<sup>2</sup> Excess uterine activity may result in fetal compromise if it persists long enough to limit the blood flow in the fetal placental unit, leading to fetal hypoxia and hypoxemia. Operative delivery, particularly cesarean delivery, is associated with increased maternal morbidity, specifically, thromboembolic disease, hemorrhage, infection, and prolonged recovery time.

The most common reason for labour induction is postterm pregnancy. Postterm or postdates pregnancy has traditionally been defined as any pregnancy that has exceeded 284 days



duration and occurs in 7% of all pregnancies.<sup>3</sup> The etiology of most postterm gestations is often unknown however primiparity and a history of previous postterm pregnancy are the 2 most common risk factors.<sup>3</sup> Risks of postterm pregnancies include increased meconium aspiration, macrosomia and stillbirth.<sup>3</sup> The increase in perinatal morbidity and mortality associated with postterm gestations is thought to be due to uteroplacental insufficiency.<sup>4</sup> In 1992, a Canadian multicentre randomized trial demonstrated that a policy of planned induction in women who are greater than 41 weeks' gestation was superior to expectant management, as induction of labour in this cohort was associated with a decreased rate of cesarean section.<sup>5</sup> A subsequent meta-analysis of routine versus selective labor induction in postterm patients found that routine induction after 41 weeks' of gestation was associated with decreased perinatal mortality (OR, 0.2; 95% CI, 0.06–0.7) with no increase in the cesarean section rate (OR, 1.02; 95% CI, 0.75–1.38).<sup>6</sup>

Compared with the spontaneous onset of labour, the process of inducing contractions has been shown to increase the risk of operative delivery, particularly in nulliparous women.<sup>7-9</sup> As operative delivery, particularly cesarean section, is associated with increased maternal risks, the ability to predict the likelihood of successful induction, defined as vaginal delivery is important. An efficient strategy to predict successful induction may also be useful in determining the type and regimen of cervical ripening agent to use. There are also potential economic implications in terms of limiting the length of antenatal hospitalization by obviating the need for a prolonged induction.<sup>7</sup>

The primary cesarean delivery rate in Canada continues to rise, and accounts for 22% of all deliveries.<sup>1</sup> For this reason, preventing a first cesarean delivery by reducing the risk of a failed induction has even greater significance. An accurate method of preinduction cervical



assessment that can determine a woman's likelihood of achieving vaginal birth would be welcome.

### **Pathophysiology of Cervical Ripening:**

It is widely recognised that the state of the cervix plays a significant role in predicting whether labour induction will be successful. A ripe or favourable cervix refers to a cervix that has become progressively shorter, dilated and soft in consistency, which resembles the features of a term cervix about to undergo spontaneous labour. The process of cervical ripening is a complex and dynamic one, and occurs in a continuum from early pregnancy to term.<sup>10</sup>

The physical structure of the cervix is comprised of a cellular portion and an extracellular matrix. The cellular component is predominately composed of smooth muscle and fibroblasts. These cells proliferate in early pregnancy, then progress into a quiescent phase during which physiological cell death occurs. Cellular death triggers invasion of the cervical stroma by inflammatory cells (neutrophils, cytokines) which release proteolytic enzymes to break down the extracellular matrix and effect softening of the cervix.<sup>10</sup>

The extracellular matrix consists mainly of collagen, elastin and proteoglycans. Collagen is the major component of the extracellular matrix and is organised as a triple helix which permits it to be cross linked into fibrous bundles. This gives the cervix its rigid structure, particularly in early pregnancy. As gestation advances, there is a decrease in collagen concentration as well as a breakdown in its organizational structure. The disruption in collagen structure is mediated by collagenases as well as by an increase in the proteoglycan hyaluronic acid, which allows for an increase in the water content of the cervix.<sup>11-12</sup> The extracellular matrix



also contains fibers of elastin which are arranged in a parallel configuration to collagen.<sup>10, 13</sup>

Under situations of mechanical stress as with labour, these fibres can distend to twice their length, thereby facilitating cervical dilatation.

Although the exact mechanism is unclear, cervical remodelling is also under a hormonal influence as the cervix contains receptors for both estrogen and progesterone and these receptors are down regulated at term gestation.<sup>14</sup> Particularly, antiprogestins have been used to facilitate cervical ripening with reasonable success.<sup>15</sup> The process of cervical ripening therefore occurs as a series of events and involves many complex interactions between the cellular and extracellular components. Overall, these interactions serve to cause decreased collagen concentration and disruption of collagen architecture, thereby allowing increased water content and resulting in a softer and more distensible cervix.



## CHAPTER 2: Background

### Cervical Scoring Systems prior to the Bishop Score

Prenatal care providers have long recognized that the progress and outcome of labour is influenced by the pre-labour characteristics of the cervix. In one of the earliest published studies in this area Calkins et al <sup>16</sup> attempted to determine clinical characteristics that predicted labour duration. Through evaluating 1250 labours, they demonstrated that only parity predicted length of labour with multiparous patients having shorter duration of labour as compared to nulliparous women.

In a subsequent multicenter study of 5700 patients which included the 1250 patients from the original study, Calkins et al suggested that a more accurate determination of labour pain effectiveness as well as resistance of the cervix would enable clinicians to more precisely estimate the duration of labour.<sup>17</sup> They proposed a scoring system for assessing cervical characteristics ranging from one for a very soft cervix to five being a firm cervix. They also devised a scoring system for contractions from one to five with one equalling poor pain and five being hard pain. One decade later, Calkins assessed 1050 patients seen at the onset of labour.<sup>18</sup> Based on his findings, he designed a dichotomous scoring system for cervical assessment. Effacement was present if the cervix was fully effaced or 3 cm dilated and absent if it did not meet this criteria. Engagement was defined as at or below the ischial spines. Cervical consistency was described as two if it was comparable to the lips or three if it was firm like the nose. Using this scoring system he determined that patients with a soft, effaced cervix and an engaged presenting part had significantly shorter duration of labour.



In 1955, Cocks proposed a different cervical scoring system based on the pre-labour characteristics of 133 patients.<sup>19</sup> A ripe cervix was defined as soft, effaced and 1-2 cm dilated (Type I and II cervix). Unripe cervixes were firm with the internal os closed (Type III and IV). Anomalous cervix was designated as Type V. Type A cervix was defined as directed posteriorly with a sacral os. Using this classification, Cocks demonstrated a greater risk of operative vaginal delivery and cesarean section in patients with an unripe cervix or with a posteriorly directed cervical os. The Cocks classification was subsequently studied by Dutton, who used it to assess 274 patients undergoing labour induction with artificial rupture of membranes.<sup>20</sup> Dutton reported that 95% of patients with Type I, 80% with Type II, 65% with Type IV, and 50% of Type III, V and Type A cervixes delivered within 72 hours.

A different cervical scoring system was developed by Garrett<sup>21</sup> in 1960 who defined a favorable cervix as being able to admit three fingers or two fingers if also well-effaced. A cervix in nulliparous patients was ripe if it could admit one and a half fingers, was soft and well effaced. In his study, successful induction, defined as onset of labour within 48 hours of amniotomy, was achieved by 96% of patients with a favourable cervix versus 63% with an unfavourable cervix. Although all these studies attempted to establish a more standardized approach to pre-labour cervical assessment, as the digital exams were performed by a single observer in these studies, they have limited generalizability. As well, these assessments were generally done via rectal examination, which would not have clinical application to the way preinduction cervical assessment is performed today.



## **The Bishop Score**

In the 1950's, Bishop studied 1000 women undergoing elective labour induction with artificial membrane rupture and intravenous oxytocin to determine the clinical characteristics that were associated with a successful induction.<sup>22</sup> He reported the duration of induction was influenced by cervical dilatation, effacement and fetal station but only in multiparous women. He suggested that elective labour induction should only be offered in the presence of certain clinical criteria. Specifically, the patient should be multiparous with a cervical dilatation of at least 3 cm and effacement of greater or equal to 60% with the fetal station at -1 or lower. In this study he also noted that prelabour cervical assessment should be made by vaginal exam rather than by rectal examination, which was a change from previous published studies in the area.

Based on the findings of his first study, Bishop went on to develop a scoring system for preinduction cervical assessment.<sup>23</sup> This system was specifically designed for elective induction of labour and prior to considering induction, minimal basic criteria had to be met: multiparity, gestational age over 36 weeks, vertex presentation, normal past and present obstetric history and patient consent for the procedure. The score had five components and consisted of cervical dilatation, effacement, station, consistency and position. Dilatation was divided into 0, 1-2 cm, 3-4 cm and 5-6 cm. Effacement was described as a percentage and ranged from 0-30, 40-50, 60-70 and 80. Station was described as a relationship of the presenting fetal part to the ischial spine of the maternal pelvis. A score of 0 for fetal station corresponded to a presenting part 3 cm above the spine (-3), score 1 was -2, score 2 was 1 cm above or at the spines (0 cm) and score 3 was 1 or 2 cm below the ischial spines. Consistency was defined as firm, medium or soft with a



corresponding score of 0, 1 and 2 respectively. Position of the cervix was defined as posterior, mid or anterior with a corresponding score of 0, 1 or 2 respectively. (Figure 1).

Factor	0	1	2	3
Dilatation(cm)	0	1-2	3-4	5-6
Effacement(%)	0-30	40-50	60-70	80
Station	-3	-2	-1 or 0	+1 or +2
Consistency	Firm	Medium	Soft	
Position	Posterior	Mid	Anterior	

**Figure1. Modified Bishop Score**

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Bishop EH. Pelvic Scoring for elective induction. *Obstet Gynecol* 1964;24(2):267.

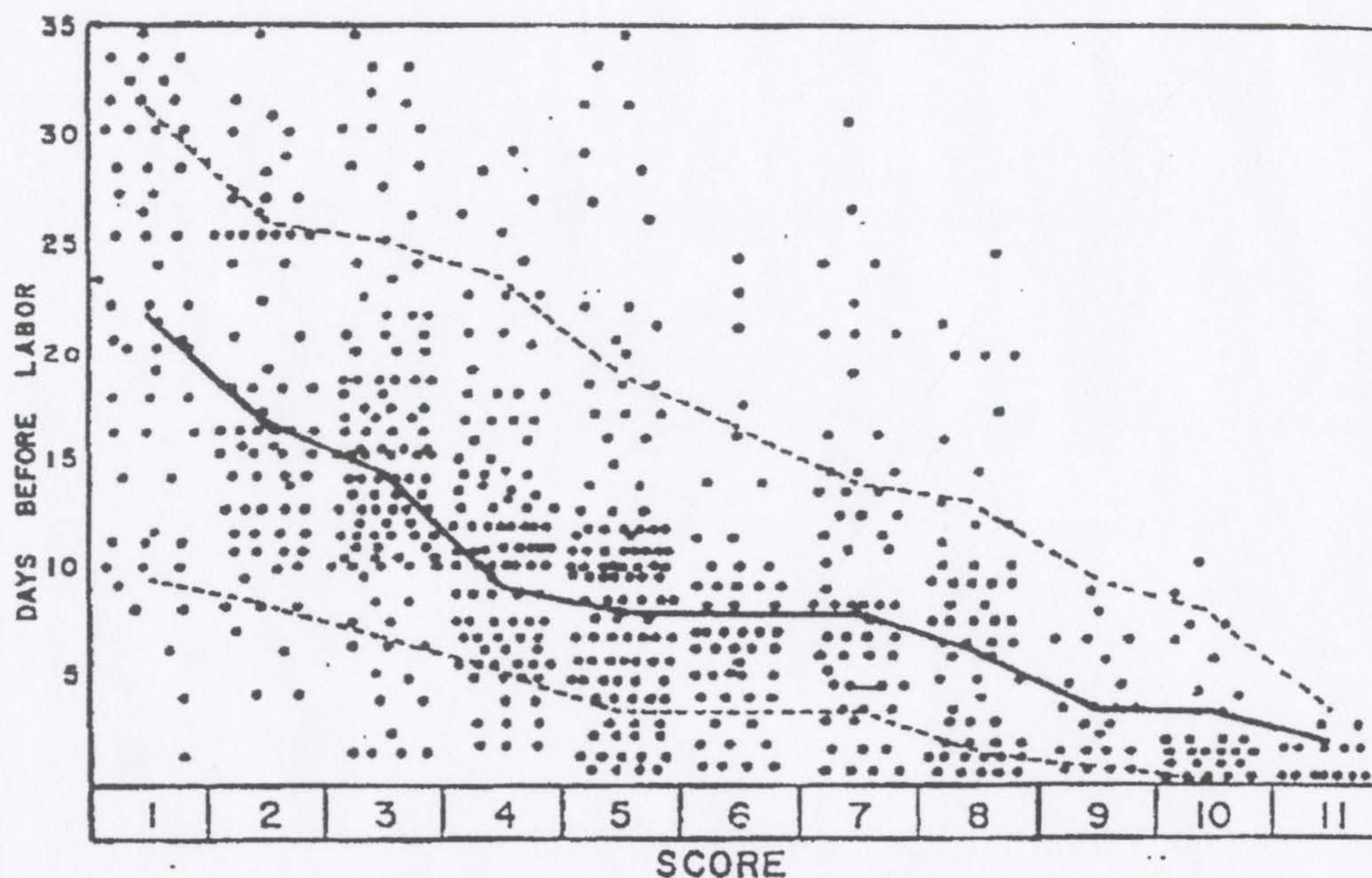
In this landmark study, Bishop recorded the pelvic scores of 500 patients who met the basic criteria for induction as outlined from his previous study, but were instead managed expectantly and allowed to go into spontaneous labour. His study found that the interval from the time of the cervical assessment to the spontaneous onset of labour was directly related to the pelvic score with the higher the score, the shorter the interval (Figure 2). Using this pelvic score, Bishop experienced no failed inductions with a score greater than 8 and found that the mean duration of labour in these patients was under 4 hours. Based on the findings of his studies, he suggested that this pelvic scoring system could have several clinical applications, with the most important one determining the optimum time to schedule elective induction, as well as timing an elective cesarean section in order to minimize any potential risks for prematurity. This would



have been an important consideration at that time, since this paper was published more than a decade prior to the use of obstetrical ultrasound to assess gestational age. Bishop also highlighted that patients of preterm gestation with a favourable cervix (high Bishop score) were at risk of preterm delivery; therefore, the pelvic scoring assessment may be useful to initiate the appropriate management of these high-risk patients.

Limitations of Bishop's study include that it was an examination of 500 patients by a single observer and therefore may not be generalizable to other physicians and centers. This is particularly an issue since certain assessments of the score, particularly effacement and station, may be subject to greater degrees of intra and inter observer variability. A strength of Bishop's study is that patients were required to meet basic criteria prior to the preinduction cervical assessment and this way minimize heterogeneity in the study population. Bishop's study included only patients who could be considered for elective induction. Conditions such as pre-eclampsia, malpresentation and spontaneous rupture of membranes which could potentially confound labour outcomes were excluded and this allows a more clear interpretation of the true influence of the pelvic score as it relates to the onset and progress of labour.





**Fig. 2.** Relation of total pelvic score and spontaneous onset of labor. Dotted lines equal 80% confidence limits, solid lines represent time to onset of labor.

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Bishop EH. Pelvic Scoring for elective induction. *Obstet Gynecol* 1964;24(2):267.

### Other Pelvic Scoring Systems

Following the publication of Bishop's landmark paper, other investigators also developed pelvic scoring systems for preinduction cervical assessment. In 1966, Burnett described a numerical system for predicting successful induction.<sup>24</sup> The score included the same five cervical components as in the Bishop score with some modifications. In Burnett's score, effacement was described as centimeters rather than a percentage and ranged from the uneffaced or greater than 1.5 cm long to effaced and less than 0.5 cm. As well, the definition for dilatation and engagement was simplified with only three categories for each, less than 1.5, 1.5 to 3 and 3



cm for dilatation and station -2, -1 or greater than 0. In this study, 100 cases of induction were examined retrospectively over a six-year period. All patients were induced with oxytocin with artificial membrane rupture only after adequate contractions were established. Patients were classified into four groups according to the preinduction score: 0 to 3, 4 to 5, 6 to 8 and 9 to 10. This study found that 89% of the patients had scores over 6 and none less than 6. The results of the study revealed that 80% of patients with a Burnett score of 9 to 10 delivered within two hours of membrane rupture. Ninety percent of patients with a score of 6-10 delivered within six hours and more patients in this group required increasing oxytocin concentrations to achieve successful induction. The remaining 20% of patients with a Burnett score of 9 to 10 delivered within four hours of beginning induction. The groups with a score of 4 to 5 and 0 to 3 had prolonged labours and time to delivery, which ranged from sixteen to eighteen hours in the 0 to 3 group and four to eighteen hours in the group with scores of 4 to 5. However, these groups had smaller numbers of patients with only three patients in the 0 to 3 group and eight in the 4 to 5 group.

This study looked at patients undergoing induction for medical indications and not just for elective reasons. A limitation of this study is that there was a significant difference in number of patients in each group. Specifically, the group of patients with a score of 0 to 3 had only three patients and the group of score of 4 to 5 had eight patients; therefore, the study has insufficient power to interpret the results for these cohorts of patients. Also, it is unclear to determine from the paper who did the pelvic assessments and this may limit the generalizability of this study.

Also in 1966, Freidman et al evaluated the Bishop score as a tool to determine prelabour inducibility as well as to predict the course of labour.<sup>25</sup> This study involved 408 multiparous



patients with 343 induced electively. The authors used Bishop's criteria to select candidates for elective induction. All inductions were done with oxytocin and artificial membrane rupture.

Overall, 93.4% of patients had a successful induction with no induction failures among patients with a Bishop score of 9 or greater and there was a 20% rate of induction failures in patients with scores less than 5 and a 4.8% failure rate in the intermediate score category (5 to 8). The authors also found that an inverse relationship between preinduction score and latent phase duration with a decreased latent phase as the Bishop score increased. A shorter latent phase subsequently led to a shorter active phase and second stage of labour. Friedman et al also examined the influence of each individual component of the Bishop score on the latent phase and noted that cervical dilatation had four times the effect on latent phase duration compared with position and two times the effect compared with cervical consistency, effacement and station. Based on these observations, these authors proposed a weighted cervical score to improve the prediction of successful labour induction. Friedman subsequently evaluated the weighted score in a prospective design and found that it was not more accurate than the original Bishop Score.<sup>26</sup>

Strengths of this study include that there were similar numbers of patients in each group of scoring category. As well, these groups were comparable in terms of demographic criteria such as age, parity, gestational age, fetal weight and type of anesthesia received, which may be factors that could potentially influence the outcome of induction. A limitation of this study is that the authors did not provide details on the 27 induction failures that they had. Another potential limitation is the risk of inter and intraobserver variability that may occur due to the use of clinical examination based on subjective criteria as with Bishop's original study.

A more elaborate scoring system was published by Fields in 1966 and used criteria in addition to cervical factors to predict inducibility of the patient such as presence of vaginal



discharge, uterine contractions, estimated fetal weight and interval from the estimated date of confinement to the actual date of induction.<sup>27</sup> For multiparous patients, a fetal score of 16 was favourable with a score of 18 required for nulliparous patients. Using this score prospectively, Fields reported that patients with a score of less than 10 who were induced had an increased length of labour duration as well as an increased cesarean section rate.

### **Evaluation of Scoring Systems**

Subsequent research focused on evaluating the Bishop score as well as other pelvic scoring systems in terms of their reliability in predicting successful induction. Hughey et al evaluated the performance of five major pelvic scoring systems – Bishop, Burnett, Fields, Friedman, (simple and weighted ) to predict successful induction.<sup>27</sup> The study examined 100 patients who underwent labour induction and had a preinduction cervical assessment by one of two physicians. Failed induction was defined as delivery by Cesarean section or, any induction which was stopped with the intention to stop labour. Following delivery, each patient was retrospectively assigned five different induction scores based on each scoring system and based on results of the initial preinduction assessment of the cervix. Overall, the rate of successful induction was 88%. Although each individual system was found to be reliable if strict pre-requisites required for each system were met, the reliability decreased when these scoring systems were applied to a more unselective group of patients. In order to allow for a more standardized comparison between the systems, these authors applied the scoring systems to all 100 patients in the study without applying the specific criteria for each individual study. They also categorized patients into lower third, middle third and upper third of scores. Using this approach, the induction failure rates were 33 to 43%, 4 to 9% and 9 to 22% in patients with scores in the lower, middle and upper third of scores respectively.



The authors then added their own modifications to the scoring systems by adding points for pre-eclampsia and subtracting points for postdates, premature rupture of membranes and nulliparity. With the addition of these modifications, the authors reported an induction failure rate of 50%, 10%, and 0% for the lower, middle, and upper third respectively. A major limitation of this study is the sample size, which leads to insufficient power to have confidence in the conclusions. As well, all cervical assessments were done by one or two individuals, which limits the generalizability of this study.

In summary, although a systematic approach to preinduction assessment with a pelvic examination may improve the ability to predict successful induction in patients with a very high score or favorable cervix, it has poor performance in patients with an unripe cervix and the results are not consistently reliable. The subjective nature of pelvic examinations also increase the potential for inter and intra-observer variability and also limits the generalizability of the previously published studies. A more objective and accurate method of assessing cervical factors is needed to improve the ability to predict successful induction.

## **Biochemical Markers of Cervical Ripeness**

### **Fetal Fibronectin**

Oncofetal fibronectin is a glycoprotein secreted by the fetal membranes and functions as a trophoblastic glue by facilitating the membrane's attachment to the decidua of the uterus. In normal pregnancy, it is detectable in the cervicovaginal secretions in early pregnancy with very low concentrations between 22 and 37 weeks gestation.<sup>29,30</sup> The presence of fetal fibronectin (FFN) in cervicovaginal fluid during this interval has been demonstrated by many prospective



observational studies to be a potent predictor of spontaneous preterm birth within 7-14 days of a positive test, particularly in symptomatic women<sup>31,32</sup> The presence of FFN in cervical secretions is thought to represent disruption of the chorion –decidual interface which may be a subclinical indicator of the onset of cervical remodelling in preparation for labour.

For this reason, many studies have also evaluated the clinical utility of this test in predicting the likelihood of successful induction at term.<sup>33,34</sup> A review of the literature by Kiss et al<sup>35</sup> examined 5 studies( 480 patients) looking at the use of FFN in predicting the onset of spontaneous labour within 2-7 days from a positive test and 3 studies (300 patients) addressing the question of FFN testing and predicting successful induction. In this review, only women over 37 weeks' gestation were considered, and women with a history of previous cesarean delivery were excluded. A positive FFN was found to have 69-96% sensitivity in predicting the onset of spontaneous labour. Among women undergoing labour induction, a positive FFN was associated with a shorter induction to delivery interval, decreased amounts of prostaglandin required for cervical ripening and decreased cesarean delivery rate. Although these results suggest that FFN may be a useful marker in predicting the outcome of induction at term, these studies are limited by heterogeneity in patient population in terms of gestational age (37-42 weeks), types and dosing regimens of induction agents used, as well as in outcomes assessed such as FFN sampling to delivery interval. There was also variation in what constituted a negative test.

Recently, Yeast et al<sup>36</sup> conducted a multicentre trial to evaluate the test performance of FFN in 875 nulliparous women with an unfavorable cervix undergoing labour induction at term. In this study, women with a positive FFN test were significantly more likely to have a vaginal delivery within 24 hours ( $P<0.0001$ ) and 48 hours ( $P=0.007$ ) and were less likely to have a



cesarean birth ( $P=0.011$ ). The strengths of this study include the large sample size and the inclusion of a cohort at high a priori risk of cesarean delivery - nulliparous women with an unfavorable cervix. However, as this study involved American centres only, it may not be generalizable to our Canadian population which has a different socioeconomic and ethnic profile.

The utility of the FFN test in predicting successful labour induction appears promising. However, the limitations of the published studies to date suggest it should not be used as a stand alone test in predicting successful labour induction.

### **Phosphorylated Isoforms of Insulin like Growth Factor Binding Protein-1**

Insulin like Growth Factor Binding Protein-1 (IGFBP-1) is made by decidual cells and as the fetal membranes start to detach from the decidua parietalis, small amounts of IGFBP-1 will leak out through the cervix and into the vagina. Recently, an immunoassay has been developed (Actim Partus<sup>TM</sup>, Medex Biochemica, Finland) to detect the presence of this protein in cervical secretions with the idea that a positive test indicates a disruption of the chorion decidual interface as the cervix begins to ripen. As with fetal fibronectin, the test was originally developed to assess premature cervical change and not specifically designed to assess cervical ripening at term. In the preterm population, several studies have reported that low levels of IGFBP-1 are associated with a decreased risk for preterm birth with a negative predictive value of 88.9 to 90%.<sup>37-39</sup> As with the fetal fibronectin assay, the high negative predictive value of this test has important clinical utility as it could potentially avoid unnecessary intervention and hospitalizations in women presenting who threatened preterm labour who were found to have a negative test.



With regards to term gestation, there has been only one published study that specifically evaluated this test to predict preinduction cervical ripeness. Nuutila et al <sup>40</sup> measured IGFBP-1 in the cervical secretions of 64 women prior to labour induction at term. The outcome measure in this study was cervical ripeness, which was defined as Bishop score  $\geq 6$ . This study reported that the median IGFBP-1 concentration in women with a ripe cervix was four times higher than in those with an unripe cervix ( $P=0.004$ ). Additionally, the concentration of IGFBP-1 in the cervix increased eight times following administration of the first dose of PGE<sub>2</sub> ( $P=0.001$ ). The authors suggested the mechanism of increased levels of IGFBP-1 in cervical secretions when with a ripe cervix is thought to be related to mechanical stress due to increased myometrial activity or possibly proteolysis and a local inflammatory reaction leading to disruption of the chorion -decidual interface.

A limitation of this study is that the outcome measure used was cervical ripeness (a less than gold standard), and not a labour or delivery outcome, thereby limiting its' reliability. As well, the small sample size causes an increased Type II error. Another limitation of this Actim Partus test is that there is a potential for false positive results in the presence of bleeding or with occult ruptured membranes. In summary, as with fetal fibronectin, there is insufficient evidence currently to recommend the use of Actim Partus as a stand-alone test to predict successful labour induction.



## Transvaginal Ultrasound

Initially, clinical applications for transvaginal ultrasound focused on gynecology and included assessment of endometrial and adnexal anatomy and pathology as well as evaluation of the endometrium. In 1996, Iams et al examined patients with transvaginal ultrasound and found a correlation between ultrasound measurement of cervical length and the risk of preterm delivery.<sup>41</sup>

A potential advantage of transvaginal ultrasound versus digital examination for assessment of cervical length is that a sonographic measurement may decrease the subjectivity associated with a clinical assessment of cervical factors. Jackson et al investigated the accuracy of digital examination and ultrasound for measuring cervical length in 20 non-pregnant women having a total abdominal hysterectomy.<sup>42</sup> Immediately prior to surgery, digital examination to assess cervical length was performed, as well as a transabdominal and transvaginal ultrasound to assess cervical length. Following the abdominal hysterectomy, the pathology specimen was measured with a ruler by a pathology resident blinded to the ultrasound and digital examination results. This study found a poor correlation between digital examination and ruler measurements of cervical length ( $P=0.0001$ ) and found that digital examination underestimated the true cervical length by 1.3 cm. There was no difference between cervical length estimations made by the ruler and either ultrasound technique ( $P>0.9$ ). As this study evaluated non-pregnant patients specifically, it may not apply to pregnant patients, as physiologic changes of pregnancy may affect cervical characteristics.

Other studies have also reported that ultrasound is superior to digital cervical length and specifically that transvaginal ultrasound may be superior to a transabdominal approach.<sup>43, 44</sup>



Possible reasons for the improved accuracy of transvaginal ultrasound is that the cervix can be imaged in its' entirety, whereas particularly with a closed internal os, digital examination cannot evaluate the supravaginal portion of the cervix. Also, abdominal ultrasound may overestimate the length of the cervix as the full bladder required for an adequate acoustic window causes a false elongation of cervical length.<sup>45</sup> Imaging may also be difficult if the patient is obese.<sup>43</sup>

An instrument that could more accurately assess cervical length may be of value in other clinical circumstances where cervical length is usually measured, such as preinduction cervical assessment.

In 1992, Lim et al published the first study comparing transvaginal ultrasound and digital examination to assess cervical readiness before labour induction in 81 patients at a gestational age of 37 to 42 weeks.<sup>46</sup> On the day of induction, the patients had measurements of cervical length and dilatation by transvaginal ultrasound followed by digital examination to assess the same parameters. The digital cervical assessment was done by a separate examiner blinded to the ultrasound findings. This study found that cervical dilatation as assessed by digital examination was greater than dilatation measured on ultrasound ( $P < 0.003$ ), and that digital examination significantly underestimated the cervical length (mean difference  $-0.03$  cm). This study examined cervical parameters only and did not evaluate labour outcomes, which is the most important outcome measure in studies evaluating induction of labour. Therefore, this study has limited value in interpreting the usefulness of transvaginal ultrasound to assess cervical status preinduction as no objective outcome measure such as time to active labour or time to delivery was studied.

The utility of transvaginal ultrasound in assessing preinduction cervical length was also investigated by Paterson-Brown in a pilot study of 50 patients undergoing labour induction.<sup>47</sup>



An increased posterior cervical angle together with a Bishop score  $>5$  had a 100% positive predictive value for vaginal delivery. Similarly Boozarjomehri et al reported that the presence of cervical funneling independently predicted the duration of latent phase ( $P=0.0001$ ) as well as total labour ( $P=0.0001$ ).<sup>48</sup> Both these studies were limited by small sample size and therefore are at increased risk for Type 2 error. As well, the independent effect of other variables including maternal factors are difficult to assess as no regression analysis was done. The Paterson-Brown study used a posterior cervical angle, which is not a usual approach to assessing cervical parameters and ultrasounds as all other studies use cervical length and the presence of funneling. Therefore, this study would have limited generalizability in terms of the way transvaginal ultrasound is used today.

Other prospective studies evaluating transvaginal ultrasound to predict induction outcome have been inconsistent in their findings. Prior to our study, two larger studies looking at transvaginal ultrasound for preinduction cervical assessment were published. Watson et al<sup>49</sup> used regression modeling to determine independent predictors of successful induction in a cohort of 109 women. The five components of the Bishop score, parity and cervical length by transvaginal ultrasound were analyzed. Only cervical dilatation on clinical examination predicted length of latent phase labour ( $P<0.001$ ). Likewise, Gonen et al evaluated 86 patients prior to labour induction and found that only Bishop score ( $P = 0.005$ ) and parity ( $P = 0.01$ ) independently predicted vaginal delivery.<sup>50</sup>

The strength of these studies is the larger sample sizes used and the fact that they controlled for potential confounders with regression modeling. Limitations are is the wide range of gestational age in their study population, as well as more heterogeneous study population in terms of indications for labour induction. Additionally, the study by Watson et al used latent



phase duration as the outcome of interest rather than vaginal delivery. Using a more heterogeneous population could potentially affect the test performance of a diagnostic tool such as transvaginal ultrasound, particularly as other studies show there is a natural history of progressive cervical change on ultrasound as gestational age advances.<sup>51</sup>

While our study was still in progress, and prior to completion of this thesis, other studies evaluating transvaginal ultrasound for preinduction cervical assessment have been published.

Ware et al used transvaginal ultrasound to assess cervical length in 77 women at term prior to labour induction with misoprostol.<sup>52</sup> The patients also had an assessment of cervical length with digital examination. These investigators found that both Bishop score and cervical length on ultrasound had a linear correlation with the duration of labour ( $P < 0.001$  for both Bishop score and cervical length). However, multiple regression analysis revealed that only parity and ultrasound measurement of cervical length independently predicted mode of delivery. This study is limited by selection bias as they included patients at increased a priori risk for cesarean section, specifically patients with non-reassuring antenatal testing and fetal growth restriction. As it is not clear from their paper that indication for induction was controlled for in the regression analysis, these variables are possible confounding factors for the outcome of interest. Another issue with this study's design is that cervical funneling was not assessed, which is a characteristic that can be identified with transvaginal scanning that has been shown to be a potential predictor of labour duration.<sup>48</sup> As well, another limitation of this study is that all patients were induced with misoprostol, a single agent, which currently is used within research protocols only and therefore may limit the study's generalizability.

More recently, Pandis et al compared Bishop score and cervical length by transvaginal ultrasound for the prediction of vaginal delivery within 24 hours of induction in 240 women.<sup>53</sup>



Regression analysis revealed that independent predictors of vaginal delivery in 24 hours, were cervical length as assessed by digital exam ( $P < 0.001$ ) and cervical length as measured by ultrasound ( $P < .0001$ ). Strengths of this study include its large sample size and the fact that the ultrasound and digital examinations were performed by multiple examiners. However, its heterogeneous population in terms of gestational age (37 to 42 weeks) and race (only 21% Caucasian) make it difficult to generalize this result to our patient population. Additional limitations are that patients with a high a priori risk of cesarean delivery such as fetal anomaly, oligohydramnios, and fetal growth restriction were also recruited. This selection bias may have influenced the rate of vaginal delivery in 24 hours, which was 73% of this study.

In another study, Gabriel et al<sup>54</sup> measured cervical parameters with transvaginal ultrasound and Bishop score in 179 patients over 37 weeks' gestation prior to medically indicated induction. They determined that a cervical length less than 26 mm was associated with a lower Cesarean section rate among women with a Bishop score less than or equal to 5 ( $P = 0.006$ ). Strengths of this study include the large sample size and that the individuals performing the transvaginal ultrasound were blinded to the Bishop score results. A significant limitation however is the lack of regression analysis, thereby making it difficult to interpret whether the relationship between transvaginal cervical length and risk of Cesarean section is truly an independent one. As 50% of the patients in this study were nulliparous, this variable could have potentially influenced the outcome and should have been controlled for in multivariate analysis. Recently, Yang et al<sup>55</sup> evaluated transvaginal ultrasound cervical assessment in predicting the outcome of labour induction. This study compared transvaginal ultrasound to Bishop score in 105 women at 37 to 42 weeks prior to labour induction. Successful induction was defined as active labour within two days. Using logistic regression, these authors



found that cervical length as measured by ultrasound independently predicted successful induction ( $P=0.002$ ) and that only parity ( $P<0.001$ ) and transvaginal ultrasound length ( $P=0.001$ ) independently were associated with duration of labour. Strengths of this study include its' large sample size and the use of a regression analysis to control for potential confounders such as maternal age, parity and gestational age at induction. However, as this study defines successful induction as onset of labour in two days, the external validity of the study is limited, as this is not the traditional definition of successful induction used in ours and other similar populations. Another limitation is that although the test performance of the Bishop score was assessed, the individual components of the Bishop score were not analyzed independently, which makes it difficult to interpret with confidence whether a particular component of digital examination could possibly predict successful induction.

As outlined in this section, the majority of studies in this area have used a term population and have not specifically focused on the post term group. In 2003, Rane et al published two studies evaluating cervical ultrasound, cervical length and prolonged pregnancy for the prediction of induction to delivery interval as well as risk for Cesarean delivery.<sup>56,57</sup> In the first study, ultrasound was used to measure cervical length of 382 singleton pregnancies prior to labour induction. The multivariate analysis found that sonographic cervical length ( $P<0.0001$ ) as well as individual components of the Bishop score: dilatation ( $P=0.009$ ), station ( $P<0.037$ ), and consistency ( $P<0.015$ ) independently predicted delivery within 24 hours. In the companion study, these investigators measured cervical length with transvaginal ultrasound in 282 women prior to labour induction.<sup>57</sup> There was an independent relationship between cervical length and risk for Cesarean delivery with a regression model demonstrating that the risk of cesarean birth increased by 10% for each 1 mm increase in cervical length. Subsequently this group went on to



publish the single largest study evaluating transvaginal ultrasound for preinduction cervical assessment.<sup>58</sup> The study involved 604 women between 35 to 40 weeks' gestational age who underwent digital examination as well as ultrasound assessment of cervical characteristics before labour induction. In evaluating the test performance of ultrasound and Bishop score, they found that ultrasound was 89% sensitive in predicting vaginal delivery within 24 hours as compared to Bishop score, which only had a 65% sensitivity. Multivariate analysis also revealed that independent predictors of vaginal delivery within 24 hours were posterior cervical angle ( $P=0.001$ ), ultrasound assessed cervical length ( $P<0.001$ ), parity ( $P<0.001$ ), body mass index ( $P=0.0034$ ), occiput anterior and occiput transverse position, ( $P=0.001$ ) for occiput posterior position. Strengths of this study included prospective design and a large sample size, as well as the use of the clinically relevant outcome of vaginal delivery within 24 hours. Limitations included heterogeneous population in terms of the wide range of gestational age used (35 to 42 weeks). This study also suffers from selection bias as eligible patients included those who were induced for antepartum hemorrhage, hypertension and fetal growth restriction, all conditions which increased the likelihood for cesarean delivery.

In summary, the studies published in the area of transvaginal ultrasound for preinduction cervical assessment have a range of limitations, which include heterogeneous ranges of gestational ages included, selection bias in terms of indications for labour induction, as well as large variations in the outcome measures assessed. There is a need for a properly designed prospective study evaluating the test performance of transvaginal ultrasound for preinduction cervical assessment.



## **CHAPTER 3: Research Protocol**

### **Primary Research Question:**

The catalyst for this study was the fact that the currently used method for assessing preinduction cervical readiness for labor induction was inconsistent in predicting successful labour induction, particularly in women with an unripe cervix. The idea was that an instrument that could more accurately assess cervical parameters could potentially increase the precision by which preinduction cervical assessment was done. We felt that successful labour induction should be defined as vaginal delivery rather than latent phase duration or time to onset of active phase labour. Restricting the study population to post term gestations exclusively allowed us to use a relatively homogeneous population to evaluate the test performance of transvaginal sonography. Therefore, the primary research question became: Is transvaginal ultrasound more accurate than Bishop Score in predicting successful labour induction in post term pregnancy?

### **Study Setting**

The study was performed at the Grace General Hospital in St. John's Newfoundland, Canada. Of the 6,000 births that occur annually in this province, 3,000 occur at this centre. This centre is a tertiary referral centre for obstetrics and gynecology for the province and the major site for postgraduate trainees in obstetrics and gynecology at Memorial University of Newfoundland. During the study period, the labour induction rate was 30% and the cesarean delivery rate was 20%.



## Study Population

Inclusion criteria were follows: singleton pregnancy at 41 weeks' gestation or beyond in vertex presentation, with intact membranes. Gestational age determination was made with rigorous menstrual dates or an ultrasound at < 20 weeks' gestation. If the ultrasound was discrepant from the menstrual dates by over 10 days, the ultrasound estimation of dates was used. Patients with previous cesarean delivery were excluded as it was felt that this group had a higher a priori risk of operative delivery which could affect the primary outcome. We also excluded any patient with a contraindication to vaginal birth such as breech presentation or placenta previa.

## Study Design

This was a prospective observational study. Recruitment occurred primarily when patients presented for labour induction to the Labour and Delivery Unit. Eligible patients were also recruited in the Maternal Fetal Assessment Unit when presenting for fetal assessment as part of the routine management of post term pregnancy. Transvaginal ultrasound was done using a 5-9 MHz transducer (Advanced Technology Laboratories, Bothwell, WA). The maternal bladder was emptied prior to the ultrasound and care was taken not to compress the cervix with the probe. Measurements of the cervical length, cervical dilatation and the presence of a cervical funnel were performed. All measurements were made in the sagittal plane. Cervical length was measured along the length of the endocervical canal with the caliber placed at the internal and external cervical os, which were visualized simultaneously in the same plane. The shortest of the three measurements obtained was recorded as the cervical length (Figure 3). Cervical dilatation was measured as the maximum width of echolucency across the endocervical canal. Funneling



was defined as a U or a V-shaped indentation of the internal os (Figure 4). This measurement was taken from the apex of the funnel to the plane of the internal os. The measurements made using transvaginal ultrasound were done three times, with an additional measurement made while manually applying suprapubic pressure to the maternal abdomen to assess cervical response to increased abdominal pressure. Labour induction was begun within an hour of the transvaginal assessment.

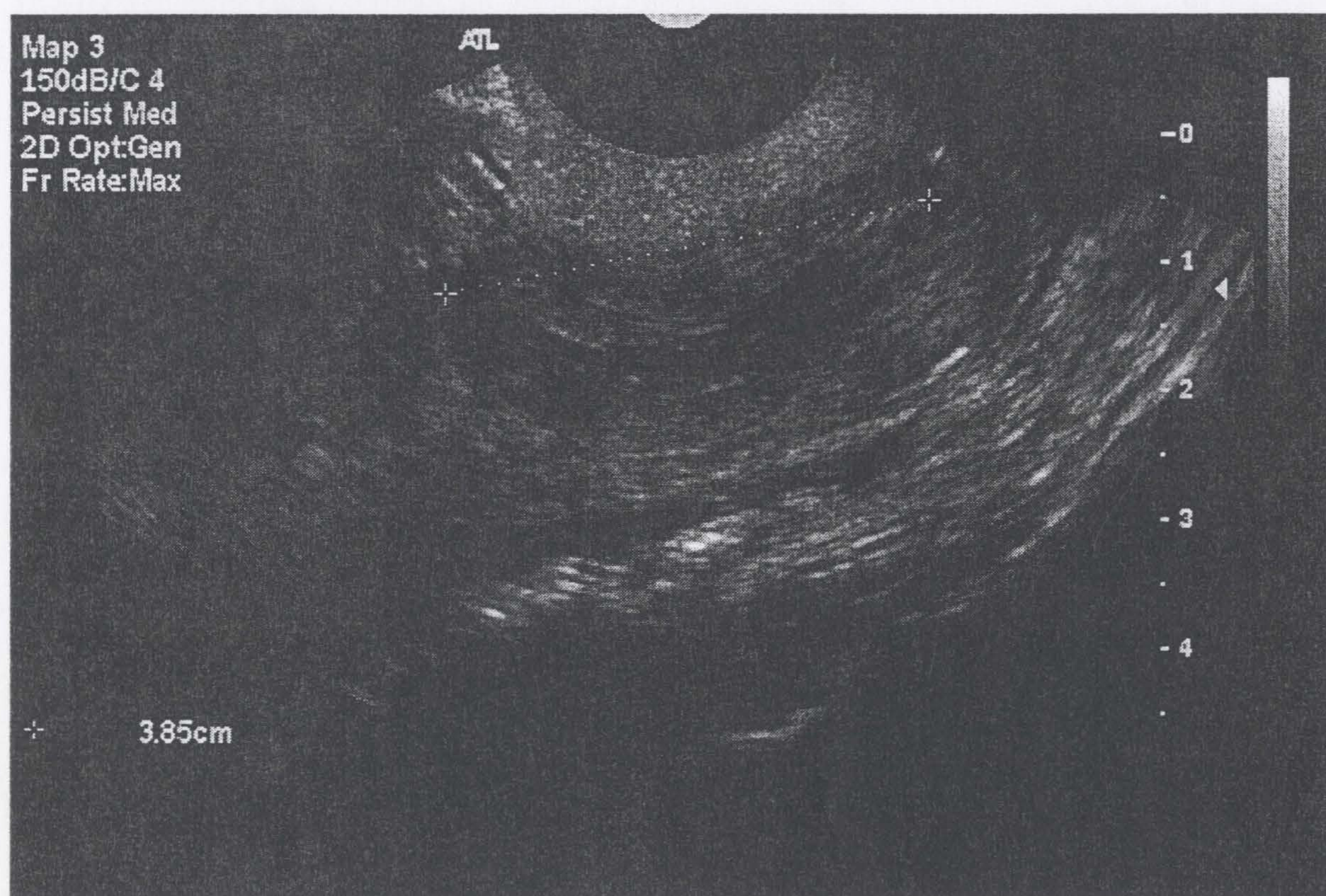


Figure 3. Transvaginal Ultrasound: Example of an uneffaced cervix



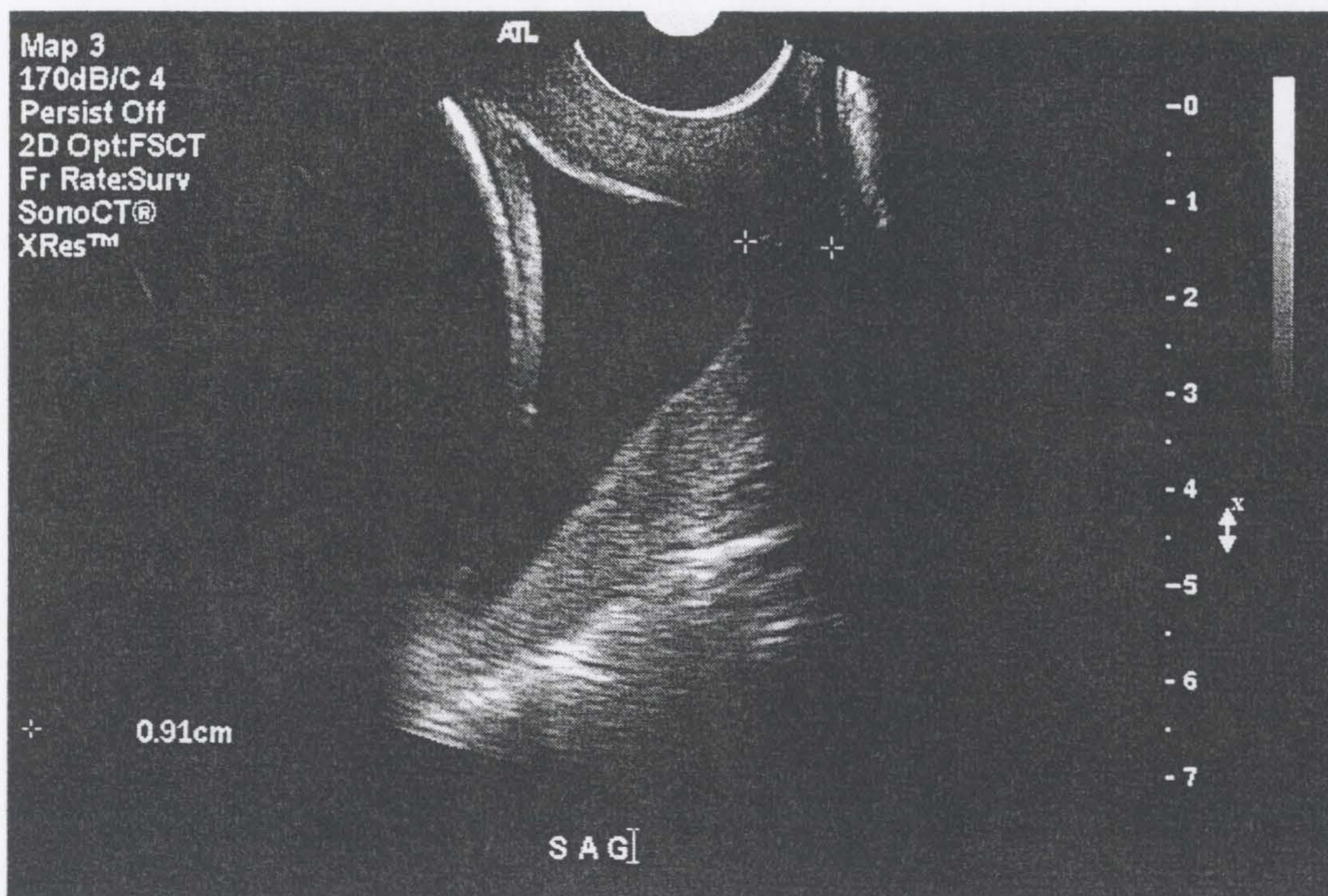


Figure 4: Transvaginal ultrasound: example of effaced cervix with funneling.

Immediately prior to labour induction, a digital examination of the cervix was performed by the resident or consulting physician in Labour and Delivery to assess the five components of the Bishop Score<sup>23</sup>: cervical dilatation, effacement, consistency, position and fetal station. The physician doing the pelvic examination was blinded to the results of the preinduction cervical assessment made by transvaginal ultrasound. Provided the fetal status remained reassuring, the patient then underwent labour induction with an induction agent determined by the attending physician. The conduct of labour and delivery, including time of amniotomy, need for oxytocin augmentation, use of analgesia and regional anesthesia was left to the discretion of the attending obstetrician on the labour ward.



## Induction Agents

During this study, patients were induced with either dinoprostone (prostaglandin E<sub>2</sub>) vaginal or cervical gels which were commercially available agents, amniotomy, oxytocin or misoprostol, which is a synthetic analogue of prostaglandin E<sub>1</sub>. Patients receiving misoprostol did so within the context of ongoing randomized controlled trials comparing 50 mcg of oral versus vaginal misoprostol in dose intervals of 4 hours or more. Dinoprostone was given as a 1 or 2 mg dose into the vagina every six hours (Prostin<sup>TM</sup>) or was administered into the cervical os every six hours as a 0.5 mg dose. (Prepidil<sup>TM</sup>) Controlled released dinoprostone (Cervidil<sup>TM</sup>) was given as a vaginal suppository and removed at the onset of regular contractions. Oxytocin was given as a continuous intravenous infusion as per the routine protocol of the hospital. Typically patients assessed as having a long, firm closed cervix received prostaglandin for cervical ripening and induction, whereas patients with a favorable cervix that was dilated and effaced were managed with amniotomy, with oxytocin infusions initiated if no active labour occurred within one hour.



## Sample Size Calculation

This study was designed to evaluate the test performance of transvaginal ultrasound in predicting successful labour induction in post term pregnancies. The primary outcome of interest was the rate of vaginal delivery. The sample size was calculated based on confidence interval around the estimated positive predictive value of transvaginal ultrasound and assumed Type I error of .05 and a margin of error of 10.<sup>59</sup> the proportion (P) used in this formula was 0.5 as this was the most conservative estimate in terms of an N number needed. Using this formula for test performance, 96 vaginal deliveries were required. Given the approximate 20% Cesarean section rate at our centre at the time, it was anticipated that 120 patients would need to be recruited to provide 96 vaginal deliveries.

$$N = Z^2 \alpha_2^2 (p)(1-p)/r^2$$

$$Z \alpha_2^2 = 1.96$$

$$P = 0.5 \quad 1-p = 0.5$$

$$r = 0.1 \text{ margin of error (1/2 the confidence interval)}$$

$$P = \text{estimated positive predictive value}$$

$$N = \text{sample size}$$



## **Outcome Measures**

The primary outcome measure was the rate of vaginal delivery. Secondary outcomes assessed the frequency of active labour in 12 hours, vaginal delivery in 12 and 24 hours, duration of the latent phase and induction to delivery interval. Active labour was defined as regular uterine contractions with a cervical dilatation of at least 4 cm and effacement of 70%.

## **The Visual Analogue Pain Scale**

While the study was already in progress, it was determined that it would also be important to assess patient discomfort with transvaginal ultrasound versus digital examination. Therefore, the study was modified to include a visual analogue pain scale for the last 40 patients recruited into the study. The pain scale used was an instrument already validated in the medical literature.<sup>60</sup> The scale used was 10 cm in length with a 0 cm mark corresponding to no pain and 10 cm corresponding to extreme pain. Study patients were instructed to draw a line through the scale at a level, which reflected their degree of discomfort.

## **Analysis**

Receiver operating characteristic curves (ROC) were constructed to determine appropriate cutoffs for transvaginal ultrasound cervical measurements. Two by two contingency tables were constructed and univariate analysis was performed with Chi Square or Fisher's Exact Test as appropriate to compare the categorical variables from Bishop score and transvaginal ultrasound. As this study was assessing transvaginal ultrasound as a diagnostic test for predicting successful labour induction, the primary and secondary outcomes were used as the gold standards for the two by two tables. Paired student t test was used to compare patient discomfort (as assessed by visual analogue scale) with transvaginal ultrasound and digital



examination. All statistical analyses was performed by Statistics 4.1 (Analytical Software, Tallahassee, Florida). Stepwise linear and logistic regression was performed to determine which variables independently predicted the primary and secondary outcomes.

### **Choice of covariates for the regression models**

In addition to examining the test performance of transvaginal ultrasound in predicting successful labour induction, the other significant outcome of interest is predicting which variables specifically are associated with a greater chance of achieving a vaginal delivery. Multiple regression is a statistical technique that allows the researcher to assess the dependency of a variable (outcome) on several independent variables (covariates). For the situation of labour induction, we considered 3 major categories of factors that could potentially influence the success of labour induction: maternal characteristics, cervical characteristics and fetal characteristics. Details of the influence of the physical characteristics of the cervix-(effacement, dilatation, position station and consistency) on induction outcomes have been described in detail in Chapter 2. Many studies on labour induction have reported that characteristics of the mother have an impact on the mode of delivery. Wing et al studied 1373 pregnancies in which vaginal misoprostol was given for labour induction and found that in addition to cervical dilatation and gestational age, parous women were 2 times as likely as nulliparous women to achieve a vaginal delivery ( OR 2.4[2.0-3.0] ).<sup>61</sup>

Using an obstetric database, Witter et al studied the influence of maternal and fetal characteristics on the risk of cesarean delivery.<sup>62</sup> Using multivariate analysis they determined that maternal pre- pregnancy weight (OR 1.06[1.04-1.07]), maternal height <1.57 m (OR1.56[1.32,1.85])and maternal age(OR 1.07[1.06-1.08] )were all independently associated



with an increased risk of Cesarean delivery. Additionally, they found that in term gestations, fetal (neonatal) birthweight at the upper ( $>3591\text{g}$  OR 1.60[1.30-1.96]) and lower ( $<2846\text{g}$  OR 1.68[1.31-2.15])) quartiles increased the risk of cesarean birth.

In summary our regression models contained the maternal and fetal characteristics of maternal age, weight, height, parity, and birthweight.

Cervical characteristics in the model included those evaluated on clinical as well as ultrasound evaluation of the cervix and were as follows: effacement dilatation, position, consistency, station cervical length, cervical dilatation and presence of funneling.

An additional covariate entered in the model was method of induction as many studies have reported that the type of induction agent used has an influence on the induction to delivery interval as well as mode of delivery.<sup>63</sup>

## **Recruitment**

Information about the study design was presented to the residents and obstetricians at the Annual Department Research Day. The research nurse inserviced the Labour and Delivery nurses as well as the nurses in the Maternal Fetal Assessment Unit prior to the study getting underway. Patients were recruited and enrolled either on presentation to the Labour and Delivery Unit for scheduled induction or following assessment of fetal status (biophysical profile) in the Maternal Fetal Assessment Unit (MFAU). Typically, patients at our centre with a gestational age of 41 weeks or beyond were referred to the MFAU for a biophysical profile so those who were found to have non-reassuring testing could be scheduled for induction on a more urgent basis. The biophysical profiles were done by one of two nurses in the MFAU and the transvaginal ultrasounds were done by two of the study investigators. Based on the recruitment



rates with previous labour induction studies at this centre, it was anticipated that over 80% of eligible patients who were approached would agree to participate.<sup>64,65</sup>

## **Ethics**

The Human Investigation Committee of Memorial University as well as the hospital Ethics Committee approved the study protocol. Informed written consent was obtained from all study patients who agreed to participate. Consent was taken by the resident on call in the Labour ward, or by one of the study investigators at the time patients presented for ultrasound assessments in the MFAU. Patients were informed that they could withdraw from the study at any time and their care would not be affected. As well, patients were informed that no information identifying them individually would appear in any publications that resulted from this study. Outcome data that was collected as well as the hard copy images of transvaginal ultrasounds were kept in the study nurse's office in one file.

## **Budget**

In 1997, the study investigators were successful in receiving funding from the Association of Professors of Obstetrics and Gynecology (APOG) through the APOG – Serono Resident Research Competition. This competition awarded a maximum of \$5,000 annually to promote research for postgraduate trainees in obstetrics and gynecology. Subsequently, an additional \$1,000 in funds was received in a grant from the General Hospital Health Foundation. The budget was used to provide funding for the study nurse who was responsible for collecting the outcome data and maintaining the database. It was also used for supplies pertaining to transvaginal ultrasound and for travel to present the study results at a national meeting.



## CHAPTER 4: Results

### Results

In this study period, 122 women were enrolled. Data was available for 120 of these 122 women with the transvaginal ultrasound data unavailable for 2 women. Two additional women were recruited to provide the required sample size. As this was a prospective observational study and not an interventional trial, this was felt to be an acceptable action. Vaginal delivery was achieved by 98 women (80%).

The demographic characteristics of the study population are described in Table 1.

**Table 1 Demographic characteristics of study patients.**

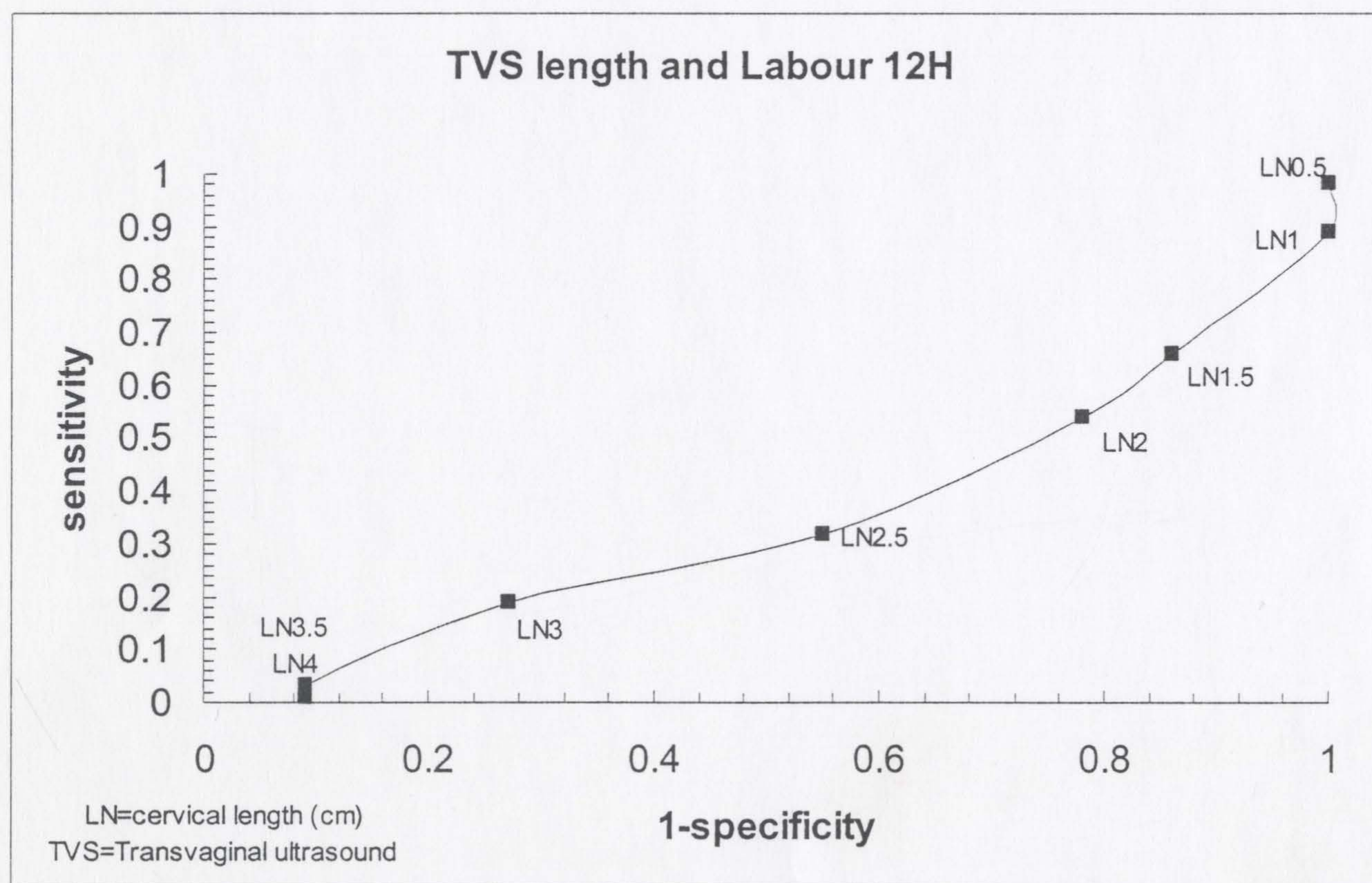
Characteristic	
Age (years)	27.9 [5.2]
Weight (cm)	164.1[12.8]
Height (kg)	89.6[18.5]
Gestational Age (days)	288.7[2]
Parity	
Nulliparous	78(64)
Multiparous	44(36 )
Ethnicity	
Caucasian	121(99.2)
First Nations	1
Induction Method	
Misoprostol	50(40)
Vaginal Dinoprostone gel	34(28.3)
Oxytocin and Amniotomy	18(15)
Amniotomy	18(15)
CR Dinoprostone	2(1.7)

Results presented as mean [standard deviation] N(%)

CR=controlled release

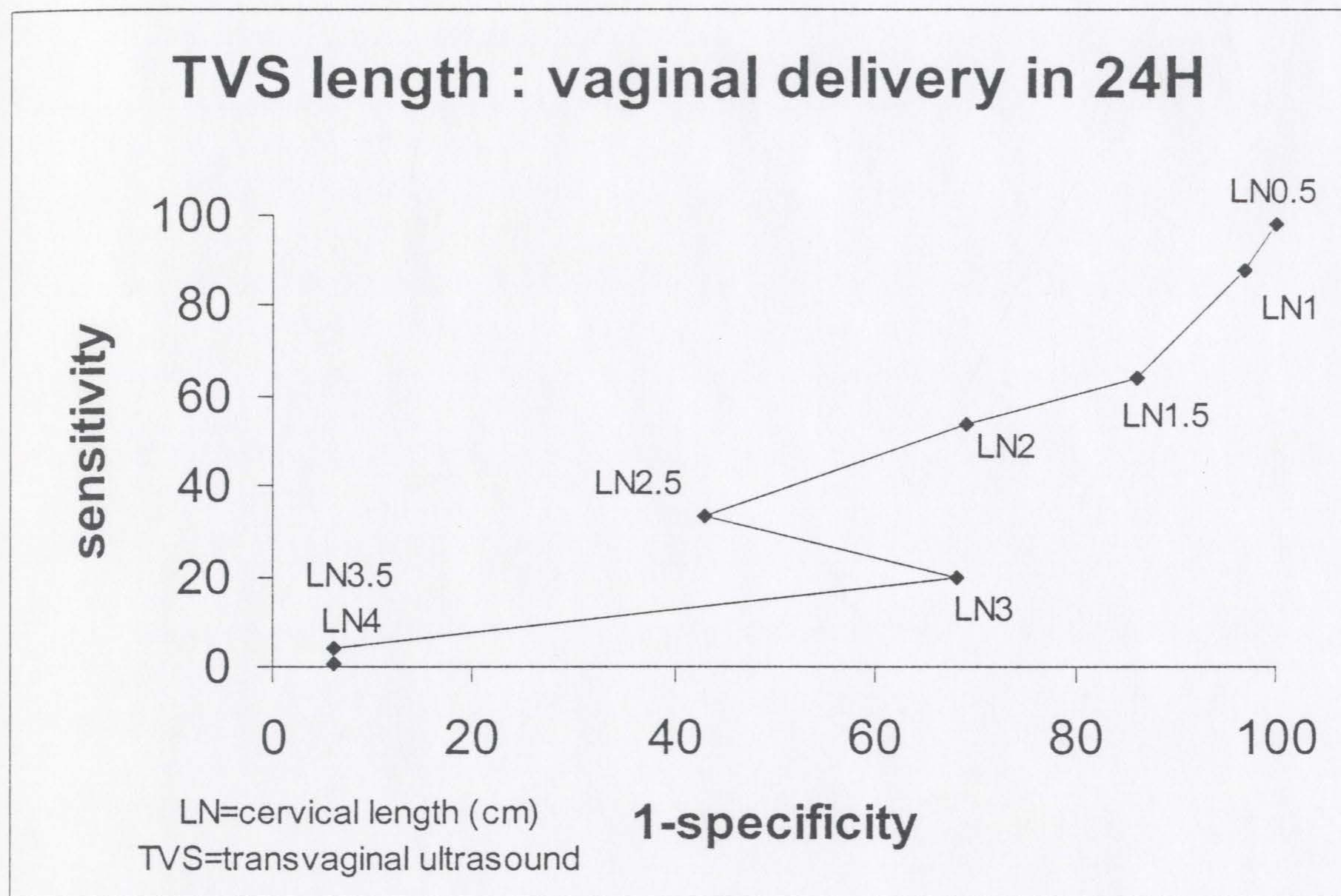


The ROC curves failed to identify an appropriate cutoff for continuous variables of the ultrasound cervical measurements. Therefore these variables were analyzed as continuous variables in the multivariate analysis. The curves for the transvaginal ultrasound measurements are illustrated through Figures 5-7. Curves were constructed for cervical length only as cervical dilatation was not well assessed by transvaginal ultrasound. There were many circumstances where the cervix appeared closed on ultrasound but was subsequently found to be dilated on digital exam.

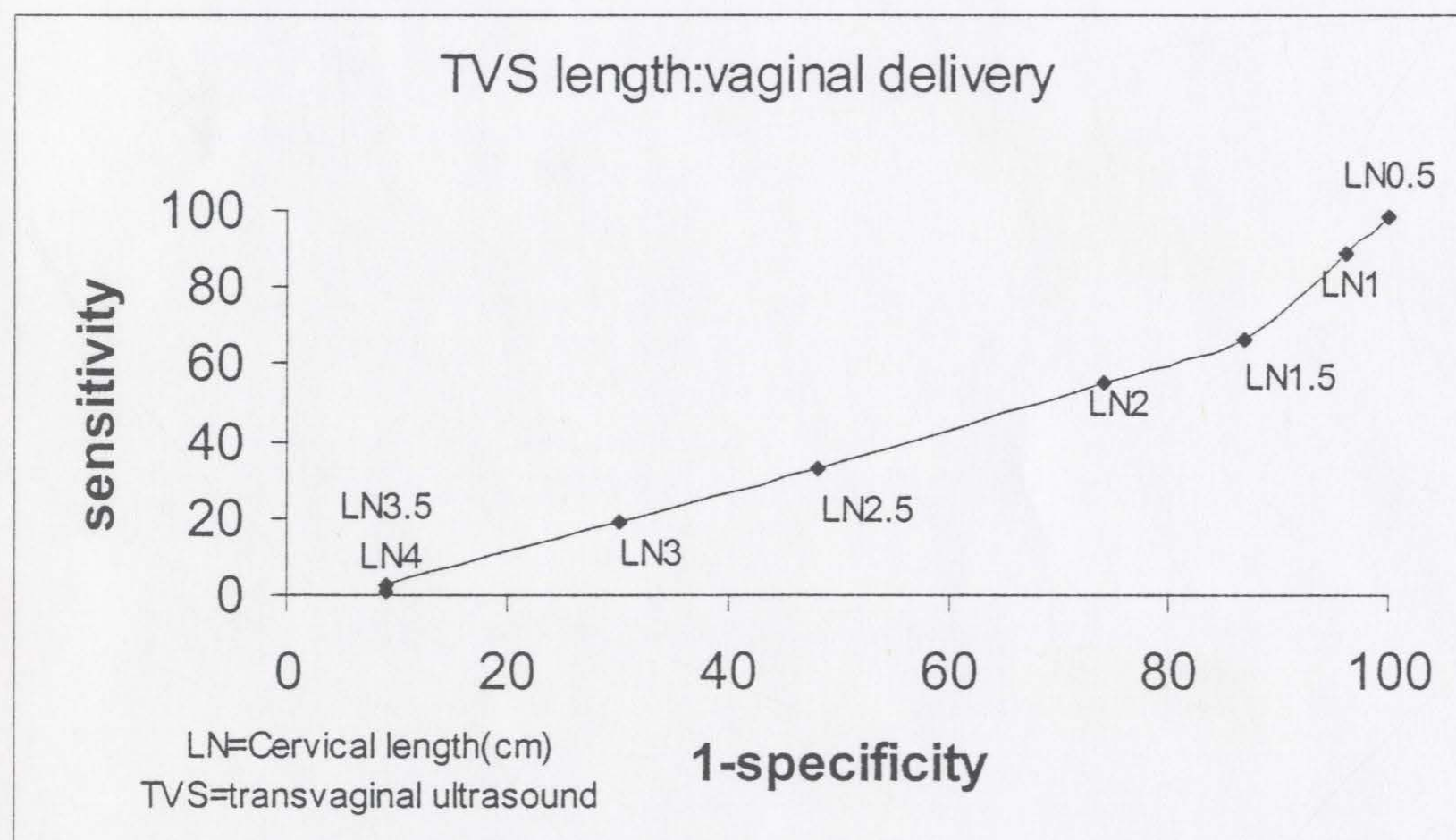


**Figure 5. ROC Curve: Transvaginal Ultrasound Length and Active Labour in 12H**





**Figure 6. ROC Curve: Transvaginal Ultrasound Length and Vaginal Delivery 24h**



**Figure 7. ROC Curve: Transvaginal Ultrasound Length and Vaginal Delivery**



Dependent variables for logistic regression were vaginal delivery, vaginal delivery in 12 and 24 hours, and active labour in 12 hours. Linear regression analysis was performed using latent phase duration and induction to vaginal delivery interval as dependent variables. Covariates which were inserted into the regression model for each of these outcomes were as follows: the Bishop score and each of its' components, sonographic cervical length, dilatation, presence of funneling, maternal age, weight, height, gestation, parity, and method of induction.

Independent predictors of successful induction (vaginal delivery) are described in Table 2 and include Bishop score, cervical position and maternal age. No ultrasound variables significantly predicted the primary outcome.

**Table 2.** Factors Predicting Vaginal Delivery

Variable	P*	OR (95% CI)
Bishop score	.001	2.98 (1.71, 5.20)
Cervical position	.009	4.35 (1.41, 12.50)
Maternal age	.013	1.15 (1.01, 1.30)

OR = odds ratio; CI = confidence interval.

Only significant variables have been listed ( $P < .05$ ).



Although no appropriate cutoff for transvaginal ultrasound variables were identified, Table 3 outlines the test performance of transvaginal ultrasound to assess preinduction cervical length and funnelling.

**Table 3.** Test Performance of Transvaginal Ultrasound in Prediction of Successful Induction

Characteristic	Sensitivity	Specificity	PPV	NPV
<b><u>Cervical Length</u></b>				
5 mm	98	0	80	0
10 mm	89	4	80	9
15 mm	66	13	76	8
20 mm	55	26	76	12
25 mm	33	52	74	13
30 mm	19	70	72	17
35 mm	3	91	60	18
40 mm	1	91	33	18
<b><u>Funneling present</u></b>	63	61	87	28

Variables significantly associated with the secondary dichotomous outcomes are shown in Table 4. Maternal weight, cervical dilatation and cervical effacement independently predicted active labour in 12 hours. Cervical dilatation, method of induction and maternal weight independently predicted vaginal delivery in 12 hours. Vaginal delivery in 24 hours was predicted independently by cervical effacement and maternal parity.



**Table 4. Predictors of Secondary Dichotomous Outcomes**

Outcome	n (%)	Variables	P*	OR (95% CI)
Active Labor (12 h)	98 (81)	Maternal weight	.004	0.96 (0.94, 0.98)
		Cervical dilatation	.005	6.08 (1.70, 21.68)
		Cervical effacement	.017	2.34 (1.16, 4.73)
Vaginal delivery (12h)	49 (40.8)	Method of induction	<.001	
		Cervical dilatation	.002	11.16 (3.17, 39.29)
		Maternal weight	.009	0.96 (0.93, 0.99)
		Gravidity	.019	2.06 (1.13, 3.77)
Vaginal delivery (24 h)	85 (70.8)	Cervical effacement	.002	2.70 (1.59, 4.57)
		Parity	.009	7.10 (2.22, 22.72)

Abbreviations as in Table 1.

\*Only significant variables ( $P < .05$ ) have been listed

Table 5 outlines predictors of secondary continuous outcomes. Factors independently associated with latent phase labour duration were maternal weight, cervical position and cervical dilatation. Predictors of induction to vaginal delivery interval were parity, cervical effacement and maternal weight. As with the primary outcome of interest, no cervical ultrasound parameters showed any significant association with the outcomes of interest.



**Table 5. Predictors of Secondary Continuous Outcomes**

Outcome	Mean (SD)	Variables	<i>P</i> *	Coefficient	Standard Error
Latent phase duration (min)	453 (440)	Maternal weight	.001	7.68	1.89
		Cervical dilatation	.005	-196.32	68.03
		Cervical position	.010	1155.2	59.02
		Method of induction	.018		
Induction to vaginal delivery interval (min)	940 (610)	Parity	<.001	-286.7	65.92
		Cervical effacement	<.001	-219.57	49.95
		Maternal weight	.006	6.67	2.38

SD = standard deviation.

\*Only significant variables ( $P < .05$ ) have been listed.

Patient discomfort by visual analogue scale was significantly less with transvaginal ultrasound compared with digital examination (mean difference 3.95,  $P < 0.001$ ).



## **CHAPTER 5: Discussion**

### **Predicting Successful Labour Induction**

Improving the precision by which cervical favourability for labour induction is determined is an important clinical pursuit, particularly for the nulliparous patient. Heffner et al examined the impact of labour induction, maternal age and gestational age on the rate of cesarean delivery in a retrospective cohort of 14,409 patients.<sup>9</sup> This study found an increased cesarean delivery rate in both nulliparous (OR 1.70[1.48, 1.97]) and multiparous (OR 1.49[1.10, 2.00]) women whose labour was induced as opposed to spontaneous onset labour. Although the odds of cesarean birth were increased regardless of parity, the absolute increase in rate of cesarean delivery was more significant in the nulliparous group (13.7 – 24.7% vs 2.4 – 4.5%). Maternal age over 35 and gestational age over 40 weeks were independent predictors of cesarean birth in nulliparous women. Our study results are consistent with these findings as we found that in addition to cervical characteristics (Bishop score, cervical position) maternal age also had an independent relationship to the likelihood of successful induction and that maternal factors including parity were significantly associated with likelihood of vaginal delivery in 24 hours. Potential reasons why advancing maternal age is a risk factor for cesarean delivery include uterine dysfunction, increased numbers of large and small for gestational age neonates, as well as a lower threshold among both patients and physicians to proceed more readily to cesarean section in older gravidas.<sup>9</sup> As our entire study population was over 41 weeks, we did not control



for gestational age in the analysis; however, the finding by Heffner reinforces the significant risk of cesarean delivery in the older nulliparous woman over 40 weeks' gestation.

None of the measurements made using transvaginal ultrasound – length, dilatation, funneling was associated with any of our primary or secondary outcomes. This is consistent with the studies by Gonen<sup>50</sup> and Watson<sup>49</sup> who also found that only clinically assessed cervical characteristics independently predicted labour outcomes. In contrast, later studies with similar or larger sample sizes have shown that ultrasound, particularly cervical length, may be useful in predicting successful induction.<sup>53,54</sup> The heterogeneity in study populations, indication for induction and gestational age at induction could possibly explain the differences in outcomes between our study and these.

We found an inverse relationship between maternal weight and duration of latent phase labour and induction to vaginal delivery interval. This is important as the proportion of overweight and obese patients in the population continued to rise including in the pregnant population. Our finding that maternal weight has an inverse influence on certain labour outcomes is also supported by a recent population based study by Joseph et al who reported that the cesarean delivery rate was significantly influenced by changes in maternal characteristics including age and weight.<sup>66</sup> A study of our own population by Crane et al examined independent predictors of successful induction as a secondary analysis of 781 women enrolled in 4 randomized trials evaluating oral or vaginal misoprostol for labour induction.<sup>67</sup> In addition to maternal height and fetal birthweight, they also found that younger maternal age ( $P=0.013$ ), multiparity ( $P<0.0001$ ) and lighter maternal weight ( $P<0.001$ ) were all associated with vaginal delivery within 24 hours, which is consistent the findings of our study. More recently, Nuthalapaty and colleagues examined the association of maternal weight with risk of Cesarean



delivery and also looked at duration of labour and rate of cervical dilation.<sup>68</sup> These authors found that maternal weight was significantly greater in women who had a cesarean birth as compared to women who delivered vaginally ( $P < 0.001$ ). Using logistic regression, they determined that among nulliparous women, each 10 kg increase in maternal weight increased the odds for cesarean birth by 17% and increased the oxytocin administration to delivery interval by 0.3 hours ( $P = 0.02$ ).

An increase in the soft tissue volume in the pelvis of overweight women leading to labour dystocia has been hypothesized by these and other authors as a potential reason why increased maternal weight adversely influences labour outcomes.

### **Test performance of transvaginal ultrasound**

The validity of a diagnostic test is measured in terms of its sensitivity, specificity and positive and negative predictive values. In the context of our study, which used an outcome measure (vaginal delivery) as the gold standard, sensitivity refers to the ability of transvaginal ultrasound to correctly identify those patients who will go on to achieve vaginal delivery, whereas specificity involves correctly identifying those who will have an operative birth. For the purposes of our study, to be clinically useful, transvaginal ultrasound would need to have a high negative predictive value when the cervix is uneffaced (cervical length  $> 3$  cm) since it is this group of patients that are at highest a priori risk of cesarean delivery and have a high sensitivity to correctly identify those women who will go on to have a successful induction. These considerations are important because in clinical practice, physicians use diagnostic tests to guide patient management particularly if the gold standard is an outcome measure.



The present study has demonstrated that the overall test performance for transvaginal ultrasound for preinduction cervical assessment and post term pregnancy is poor. This is reflected in the fact that the ROC curves failed to identify an appropriate cutoff for any of the factors assessed by transvaginal ultrasound. For the primary outcome of successful induction (vaginal delivery) the sensitivity and positive predictive value of transvaginal ultrasound measurements, specifically cervical length was high only in patients with an extremely short cervix and did not perform as well as the cervical length increased. As well, the negative predictive value of transvaginal ultrasound for prediction of vaginal delivery was poor across the entire range of cervical lengths. In other words, transvaginal ultrasound was only useful in identifying patients with a ripe cervix who would have a successful induction. In terms of cervical effacement, the Bishop score performed similarly as well with the highest positive predictive value in patients with the most effaced cervix.

In the circumstance of transvaginal ultrasound for the prediction of successful labour induction, having a high positive predictive value does not provide any additional benefit to the clinician since these levels of cervical length indicate a ripe cervix, which a clinician is able to determine equally well with a digital examination. A similar view is also held by Gabriel et al who have suggested that transvaginal ultrasound is ineffective for preinduction cervical assessment when clinical examination reveals a favorable cervix.<sup>54</sup> The additional information provided by transvaginal ultrasound may not aid the clinician in timing of induction particularly in the circumstance of the post term patient with stable fetal status where induction may not be urgent or emergent.



## Limitations

It is important to acknowledge the limitations of the present study. At the outset of the study, patients were not stratified according to method of induction. The induction agent used can influence induction duration and mode of delivery and in our study independently predicted vaginal delivery in 12 hours and latent phase duration. Pharmacologic agents used for labour induction include oxytocin, as well as the prostaglandins dinoprostone and misoprostol. In a patient with an unfavorable cervix, oxytocin is not an effective induction agent as although it promotes myometrial contractions, it is not effective for cervical ripening. Prostaglandins, in contrast, can ripen the cervix and cause uterine contractions.

A large systematic review including 70 studies reported that the PGE1 analogue misoprostol is more effective than the other pharmacologic methods of induction<sup>63</sup>. Specifically, vaginal misoprostol was associated with a shorter induction to delivery interval, reduced need for oxytocin augmentation and a reduced risk for cesarean delivery. Given these findings, it may be possible that our labour outcomes were influenced by the induction agent, particularly as half our study patients received misoprostol. We controlled for method of induction as a potential confounder in the regression models; however, the model was not designed to look at which specific agent (misoprostol or PGE<sub>2</sub>) was associated with successful induction, but more simply that choice of induction agent had an influence on the outcome of labour. An alternate way to address this question in future studies would be to create dummy variables for each agent except the one under study to determine the independent contribution of each specific type of induction agent to the outcomes of interest. The numbers of patients in each induction group were not comparable as only two patients received controlled released dinoprostone while half the study



population received misoprostol. Hence, it was not feasible in the present study to analyze test performance of transvaginal ultrasound and Bishop Score for each induction agent.

Another potential limitation is that all of the transvaginal sonographic measurements were performed by two operators (S. Chandra, J. Crane). Having an increased number of operators to do the ultrasound measurements would be advantageous, as it would increase the external validity of our study. However, this approach was not feasible at our centre since all transvaginal ultrasounds were being done by the Maternal Fetal Medicine division of which there was only one such specialist in our department. Unlike digital examination of the cervix, which is a technique that all obstetricians would be familiar with performing, transvaginal ultrasound assessment of the cervix requires additional technical training to provide reproducible results. Nevertheless, the technique for performing transvaginal ultrasound is described in sufficient detail in the "Method" section above and should be easily performed by other operators with transvaginal ultrasound skills and experience.



## **Future Research Directions**

In the patient with a closed cervix, the supervaginal portion of the cervix cannot be evaluated by digital examination and may result in an underestimation of the true cervical length. As transvaginal scanning can image a supervaginal segment of the cervix, it potentially gives a more accurate estimate of cervical length. Therefore, transvaginal ultrasound may be clinically useful in predicting successful induction in the specific cohort of patients with a closed, uneffaced cervix. As our study included multiparous and nulliparous patients, as well as patients with a wide range of cervical dilatation, this may explain why transvaginal ultrasound did not add any additional information in predicting successful induction as compared with Bishop Score. Future studies should specifically evaluate the test performance of transvaginal ultrasound in patients at the highest a priori risk of Cesarean delivery - nulliparous women with a closed, uneffaced cervix. In addition to measuring labour outcomes, future studies should also address method of induction agent used.

Another consideration when evaluating different methods of preinduction cervical assessment is that each individual method may only be capable of assessing certain cervical characteristics and not others, when there may be many factors that are important to consider that could potentially influence the likelihood of successful induction. As an example, the consistency of the cervix is a feature that can be assessed by digital examination, but not transvaginal ultrasound. A cervix that has not yet dilated but has increased water content will feel soft to the examiner, but would not be reflected as a ripe cervix according to transvaginal scanning. In this way, it can be seen that digital examination and transvaginal scanning may



each contribute different and complementary information to the overall state of the cervix. The superiority of one method of assessment over another has not been convincingly established.

In the preterm population, studies have supported that a combination of transvaginal scan, and fetal fibronectin performed better than each individual component alone in predicting preterm birth.<sup>64</sup> In term patients, the use of the combination of methods to assess preinduction cervical characteristics has recently been evaluated in two studies.<sup>65,66</sup> Reis et al used digital examination, fetal fibronectin assay and transvaginal ultrasound to assess the cervix in 134 women undergoing labour induction at term.<sup>65</sup> Regression analysis determined that only abbreviated Bishop score, defined as dilatation and effacement, (OR 2.93 [1.59 to 5.40]) and a history of previous vaginal delivery (OR 2.22 [1.24 to 3.96]) independently predicted successful induction. Likewise, Rozenberg et al assessed the cervical characteristics in 128 women at term using fetal fibronectin, transvaginal ultrasound and a Bishop score.<sup>66</sup> Outcomes assessed were the percentage of patients in spontaneous labour within a week of the assessment, as well as mode of delivery. This study found that the Bishop score > 6 (OR 2.65 ([1.09 to 6.43]) and transvaginal cervical length of < 26 mm (OR 3.18 [1.36 to 7.42]) were associated with the likelihood of spontaneous labour within seven days. A positive fetal fibronectin result was not predictive of spontaneous labour, whereas it was associated with mode of delivery (P = 0.01). Interestingly, there was no correlation between Bishop Score or ultrasound cervical length and mode of delivery.

These authors proposed that these different methods of assessing the cervix provide different physiologic data: Bishop Score and transvaginal length are markers for myometrial sensitivity for labour whereas fetal fibronectin is a marker for cervical ripening. They suggest that in some circumstances, the process of cervical and myometrial readiness for labour may not



be coordinated and failed induction may be related to cases where myometrial ripeness precedes cervical ripeness. The result is the ability to produce uterine contractions with a cervix that is not prepared for labour.

These theories provide new insight into factors involving cervical ripening. Perhaps several processes must occur in a coordinated sequence for the uterus to be sensitive to induction agents and a cervix to be remodeled to permit delivery. Further investigations on assessing preinduction cervical characteristics should focus on determining whether several processes are involved and whether a combination of modalities are required to assess this with more precision.



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## Appendix A

### INFORMATION SHEET

**TITLE :** The Accuracy Of Transvaginal Ultrasound In Predicting Successful Labour Induction In the Postterm Pregnancy .

**INVESTIGATORS :** S.Chandra M.D. , J.Crane M.D. , D.Young M.D. , G.Fox M.D.

You are being asked to participate in a research study. Participation in this study is entirely voluntary. You can withdraw from this study at any time without affecting your normal care and treatment in labour.

#### BACKGROUND

The current practice in Canada for overdue pregnancies is to offer induction of labour when you are one week overdue. Studies have shown that induction between 41 -42 weeks decreases the risk of complications to the baby.

In this center, you are evaluated for induction by means of a internal examination of the cervix , to look at factors including cervical dilatation and thickness, which are helpful in predicting whether the induction will be successful . Results of this exam may vary depending on the individual doing the assessment. Another way to assess the cervix is by a vaginal ultrasound which may give more accurate and consistent measurements since one can see the entire cervix and not just rely on an individual person's examination.

This study will attempt to determine whether vaginal ultrasound is accurate in predicting if induction will be successful in women who are overdue.

#### STUDY DESIGN

If you are scheduled for induction of labour because you are overdue ( 41 + weeks ) and you choose to enter this study , at the time of your induction you will get an ultrasound of the cervix followed by an internal exam by a different investigator. There will be no additional examinations or blood tests other than those for normal labour and delivery practice. You will remain under the care of your physician who will manage your labour and delivery as per usual. Your induction will be as per the standard method used in this center. After delivery your chart will be reviewed by the investigators of this study to get information regarding your labour and delivery.



## Appendix B

### CONSENT FORM

**TITLE :** The Accuracy Of Transvaginal Ultrasound In Predicting Successful Labour Induction In the Postterm Pregnancy

**INVESTIGATORS :** S.Chandra M.D. , J.Crane M.D.

**Supervisors :** Dr. Crane , Dr. D. Young Dr. G. Fox

You are being asked to participate in a research study. Participation in this study is entirely voluntary. You can withdraw from this study at any time without affecting your normal care and treatment in labour.

#### BACKGROUND

The current practice in Canada for overdue pregnancies is to offer induction of labour when you are one week overdue. Studies have shown that induction between 41 -42 weeks decreases the risk of complications to the baby.

In this center, you are evaluated for induction by means of a internal examination of the cervix , to look at factors including cervical dilatation and thickness, which are helpful in predicting whether the induction will be successful . Results of this exam may vary depending on the individual doing the assessment. Another way to assess the cervix is by a vaginal ultrasound which may give more accurate and consistent measurements since one can see the entire cervix and not just rely on an individual person's examination.

A vaginal ultrasound is an internal ultrasound of the cervix in which the ultrasound guide is placed in the vagina to measure the cervix.

This study will attempt to determine whether vaginal ultrasound is accurate in predicting if induction will be successful in women who are overdue.

#### STUDY DESIGN

If you are scheduled for induction of labour because you are overdue ( 41 + weeks ) and you choose to enter this study , at the time of your induction you will get an ultrasound of the cervix followed by an internal exam by a different investigator. There will be no additional examinations or blood tests other than those for normal labour and delivery practice. You will remain under the care of your physician who will manage your labour and delivery as per usual. Your induction will be as per the standard method used in this center. After delivery your chart will be reviewed by the investigators of this study to get information regarding your labour and delivery.



## FORSEEABLE RISKS AND DISCOMFORTS

Vaginal ultrasound is a safe tool in pregnancy. Most women who have had this test say it causes less discomfort than a regular internal exam .

## ALTERNATIVE TREATMENTS

Should you choose not to participate in this study you will undergo induction as per usual protocol without affecting your normal care.

## VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Should you wish, you may choose to withdraw from this study at any time without affecting your regular care and treatment.

## CONFIDENTIALITY

If you choose to participate in this study you will give the investigators permission to review your hospital records concerning your labour and delivery. No records bearing your name will be provide to anyone other than the investigators in this study . You will not be identified in publications in any manner.

### Liability Statement

"Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to participate as a subject. In no way does this waive your legal rights nor release the investigators, sponsors, or involved institutions from their legal and professional responsibilities."

To the best of my ability I have fully explained to the subject the nature of this research study. I have invited questions and provided answers. I believe that the subject fully understands the implications and voluntary nature of the study.

PATIENT ----- DATE -----

INVESTIGATOR ----- DATE -----



# Appendix C

NAME \_\_\_\_\_

## BISHOP SCORE

please circle the appropriate value for each parameter

	Points			
	0	1	2	3
Cervical Dilatation	closed	1-2 cm	3-4 cm	> 5 cm
Cervical Effacement	0-30%	40-50 %	60-70%	>80%
Fetal Station	-3	-2 to -1	0	+1 to +2
Cervical Consistency	firm	medium	soft	
Cervical Position	posterior	mid	anterior	

TOTAL SCORE \_\_\_\_\_

Done By / Date \_\_\_\_\_

Induction method : \_\_\_\_\_

length 1<sup>st</sup> stage: \_\_\_\_\_

Induction  
~~Latent Phase~~  
 Active Phase

Time of Onset

\_\_\_\_\_  
 \_\_\_\_\_

Full dilatation  
 2nd stage

Time

\_\_\_\_\_  
 \_\_\_\_\_

Outcome of delivery

SVD

Time delivery: \_\_\_\_\_

Operative Vaginal

Vacuum

Forceps

Cesarean Section

Indication \_\_\_\_\_



**DEMOGRAPHIC DATA**  
Transvaginal Ultrasound Study

Patient Name	
Chart #	
Gravida	
Para	
LMP	
EDC	
Gestational age	
BPP Score	
Amniotic Fluid Index (mm)	
Estimated Fetal Weight	
Age	
Weight	
Height	
Ethnic Background	
Episiotomy	
Laceration	vag    perineal    sphincter    rectum
Apgar Score	1 min ____ 5 min ____ cord ph ____
Neonatal weight at delivery	



# TRANSVAGINAL ULTRASOUND in POSTTERM PREGNANCY

Patient ID

LMP

EDC

GESTATION

Gravida

Para

Biophysical Profile Score

---

## Vaginal Ultrasound Measurements

Cervical Length ( cm ) \_\_\_\_\_

Cervical Dilatation ( cm ) \_\_\_\_\_

Funnelling	present	width (cm) _____	absent
		length (cm) _____	
Funnelling with suprapubic pressure	present	width (cm) _____	absent
		length (cm) _____	



Appendix D



# Memorial

University of Newfoundland

Human Investigation Committee  
Research and Graduate Studies  
Faculty of Medicine  
The Health Sciences Centre

1997 09 02

Reference #97.107

Dr. S. Chandra  
Department of OBS/GYN  
Grace General Hospital

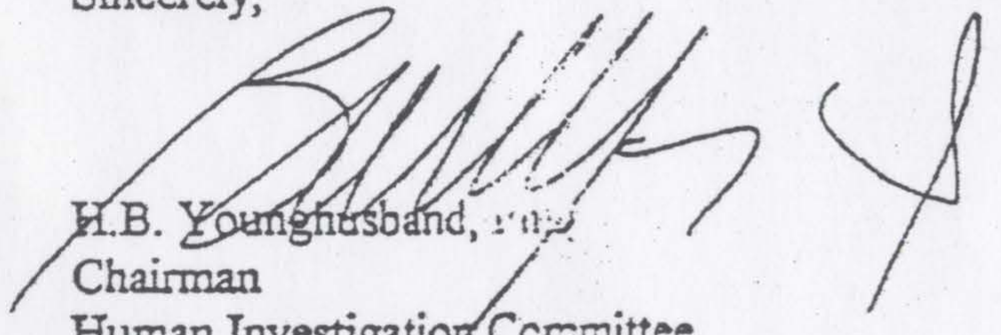
Dear Dr. Chandra:

This will acknowledge receipt of your revised consent form for the research application entitled "The Accuracy of Transvaginal Ultrasound in Predicting Successful Labor Induction in the Postterm Pregnancy".

At a meeting held on August 28, 1997, the Human Investigation Committee granted full approval of your application.

We take this opportunity to wish you every success with your research study.

Sincerely,

  
H.B. Younghusband, M.D.  
Chairman  
Human Investigation Committee

HBV/jglo

c Dr. K.M.W. Keough, Vice-President (Research)  
Dr. E. Parsons, Vice-President, Medical Services, HCC



## Appendix E

Applicant Name : SUJATA CHANDRA

### DETAILED BUDGET JUSTIFICATION

#### Personnel

Position : Research Nurse

Credentials: Bachelor of Nursing

Pay Scale: As per Collective Agreement NLNU , NHHNA and  
Treasury Board

Duties : function as part time research assistant  
data collection on patient demographics, intrapartum and  
postpartum outcome  
data entry into computer  
participate in informed consent process  
educate medical and nursing staff i.e. housestaff, labour  
and delivery nurses regarding study protocol

Salary As per payscale outlined above : \$ 19.25 /hour

3 h/week x 52 weeks total : 156 h \$3000.00

Benefits ( 25 % gross salary ) 750.75

Annual leave ( 8% gross salary ) 240.24

TOTAL \$ 3990.99

#### Materials

Examination Gloves 32.35 /100 x 2 boxes \$ 64.70 \*

Muko Jelly 6.98 / 100 x2 boxes \$ 13.97 \*

Condoms for Vaginal U/S 6.29 /12 pkg x 10 boxes \$ 62.90 \*



Applicant name: SUJATA CHANDRA

Expendables

Phone /Fax \$ 40 /month x 12 months	\$ 480.00
15 % HST	<u>72.00</u>
TOTAL	\$ 552.00

Printing

Estimated cost of photocopying

\$ 0.02 /copy x 2000 copies	\$ 40.00
15 % HST	<u>6.00</u>
TOTAL	\$ 46.00

TOTAL	\$ 4730.56
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\* HST included as per Hospital contract

\*\* computer equipment already supplied as it is available for resident use in resident resource room







